The Tuberculosis Trials Consortium

WHAT IS THE HEALTH ISSUE?

- Tuberculosis (TB) remains a domestic challenge, and continues to fuel a global epidemic. In the United States, over 14,000 cases occurred in 2003, affecting persons of all ages, both genders, and all ethnicities.
- Treatment of TB is long and complicated: treatment of TB disease requires six months or more of therapy with multiple medicines and treatment of latent TB infection to prevent TB disease requires nine months or more of therapy. The last new drugs for use in TB treatment were developed over 30 years ago. Moreover, resistance to these drugs is growing.
- Beginning in the late 1940s, the U.S. Public Health Service (USPHS) played a key role in the development of new treatment regimens for treatment and prevention of TB disease. From 1947 to 1988, the USPHS and Department of Veterans Affairs collaborated in 21 clinical studies. These trials studied the TB drugs in use today (i.e., streptomycin, isoniazid, rifampin, pyrazinamide, and ethambutol). In more recent years, maintenance of the capacity to conduct state-of-the-art clinical trials and related research in TB has diminished, and no new agents or strategies for the treatment of TB appeared.

WHAT HAS CDC ACCOMPLISHED?

In 1995, CDC initiated and funded the TB Trials Consortium (TBTC), a consortium of U.S. and international TB investigators. The TBTC is a unique public-private sector partnership involving local TB control programs, academic medical researchers, the Department of Veterans Affairs, and CDC. The TBTC's purpose is to provide scientific data that define effective TB treatment and prevention regimens in the 21st century, identify programmatically relevant research questions and carry out targeted clinical studies to investigate these questions, conduct research to improve treatment and prevention of TB among HIV-infected persons and other special populations, and promote integration of critical clinical research into the care of persons with TB in the public health setting.

The TBTC investigates the efficacy, use, and safety of new anti-TB drugs, starting with rifapentine. The TBTC is currently enrolling patients into five TB treatment trials and one TB prevention trial in 28 clinical sites; 26 percent of total patient enrollment is from sites in South Africa, Uganda, and Brazil.

The TBTC findings influenced many of the changes in the 2003 TB treatment guidelines from CDC, the American Thoracic Society, and the Infectious Diseases Society of America. For example, TBTC-Study 22 defined the appropriate use of rifapentine-based regimens for TB treatment, identified characteristics of TB patients at high risk for treatment failure or relapse, and documented the importance of using timing of culture conversion for selecting duration of TB therapy. TBTC-Study 23 determined the proper use of rifabutin with highly active antiretroviral therapy (HAART) and identified the approach for managing patients with advanced TB and HIV disease. The TBTC-Study 23 also alerted the TB community to the risk of acquired rifampin resistance in patients with advanced TB and HIV disease, and helped shape recommendations for their proper management, in conjunction with TBTC-Study 22.

WHAT ARE THE NEXT STEPS?

CDC will continue to:

- Study the development of moxifloxacin-based regimens aimed at a shorter duration of treatment.
- Study other agents to develop shorter, less toxic, and more cost-effective treatment.
- Identify the role of individual pharmacokinetic evaluations.
- Examine TB treatment issues concerning children, HIV-associated TB, and multidrug-resistant TB.

For information on this and other CDC and ATSDR programs, visit www.cdc.gov/programs. 2005